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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|---|---|---|---|---|
| 09/167,705 | 10/06/1998 | ANN MARIE SCHMIDT | 55873JPWJML | 1656 |

7590 07/08/2005

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| EXAMINER | |
|---|---|
| EMCH, GREGORY S | |

| ART UNIT | PAPER NUMBER |
|---|---|
| 1649 | |

DATE MAILED: 07/08/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 09/167,705 | SCHMIDT ET AL. | |
| | Examiner | Art Unit | |
| | Gregory S. Emch | 1649 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *25 March 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1-17* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-17* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *3/25/2005*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

## DETAILED ACTION

### *Continued Examination Under 37 CFR 1.114*

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after allowance or after an Office action under Ex Parte Quayle, 25 USPQ 74, 453 O.G. 213 (Comm'r Pat. 1935). Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, prosecution in this application has been reopened pursuant to 37 CFR 1.114. Applicant's submission filed on March 25, 2005 has been entered.

### *Formal Matters*

Claims 1-17 were withdrawn from issue in the petition decision dated March 20, 2005. Claims 1-17 are pending and under consideration.

### *Claim Rejections - 35 USC § 112*

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-17 are rejected under 35 U.S.C. 112, first paragraph, because the specification, which is enabling for a method for inhibiting inflammation in a subject which comprises administering to the subject a compound selected from the group

consisting of: an anti-EN-RAGE antibody and the V-domain of soluble RAGE polypeptide, does not reasonably provide enablement for a method for inhibiting inflammation in a subject which comprises administering to the subject a fragment of an anti-EN-RAGE antibody or a method for inhibiting inflammation in a subject which comprises administering to the subject a fragment of the V-domain of soluble RAGE polypeptide. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The claims are drawn to a method for inhibiting inflammation in a subject which comprises administering to the subject a compound selected from the group consisting of: an anti-EN-RAGE antibody or fragment thereof and the V-domain of soluble RAGE polypeptide or fragment thereof, thereby inhibiting inflammation in a subject. The claims are overly broad since insufficient guidance is provided as to which of the fragments of the anti-EN-RAGE antibody or the fragments of the V-domain of soluble RAGE polypeptide will retain the characteristics of inhibiting inflammation in a subject. Applicants do not disclose any actual or prophetic examples on expected performance parameters of any of the possible fragments of the anti-EN-RAGE antibody or the fragments of the V-domain of soluble RAGE polypeptide.

It is known in the art that even single amino acid changes or differences in the amino acid sequence of a protein can have dramatic effects on the protein's function. As an example of the unpredictable effects of mutations on protein function, Mickle et al. teaches that cystic fibrosis is an autosomal recessive disorder caused by abnormal

function of a chloride channel, referred to as the cystic fibrosis transmembrane conductance regulator (CFTR) (page 597). Several mutations can cause CF, including the G551D mutation. In this mutation a glycine replaces the aspartic acid at position 551, giving rise to the CF phenotype. In the most common CF mutation, delta-F508, a single phenylalanine is deleted at position 508, giving ride to the CF phenotype. Thus showing that even the substitution or deletion of a single amino acid in the entire 1480 amino acid CFTR protein sequence can have dramatic and unpredictable effects on the function of the protein. Additionally, it is known in the art that even a single amino acid change in a protein's sequence can drastically affect the structure of the protein and the architecture of an entire cell. For example, Voet et al. (1990) teaches that a single Glu to Val substitution in the beta subunit of hemoglobin causes the hemoglobin molecules to associate with one another in such a manner that, in homozygous individuals, erythrocytes are altered from their normal discoid shape and assume the sickle shape characteristic of sickle-cell anemia, causing hemolytic anemia and blood flow blockages (pages 126-128, section 6-3A and page 230, column 2, first paragraph). Additionally, Yan et al. teaches that in certain cases, a change of two-amino acid residues in a protein results in switching the binding of the protein from one receptor to another (Yan et al., Two-amino acid molecular switch in an epithelial morphogen that regulates binding to two distinct receptors, *Science* 290: 523-527, 2000).

Since the claims encompass methods using fragments of the anti-EN-RAGE antibody or methods using fragments of the V-domain of soluble RAGE polypeptide and given the art recognized unpredictability of the effect of mutations on protein function, it

would require undue experimentation to practice the claimed invention. See In re Wands, 858 F.2d at 737, 8 USPQ2d at 1404. The test of enablement is not whether any experimentation is necessary, but whether, if experimentation is necessary, it is undue. The claims do not set forth a functional limitation for the polypeptide fragments. Since detailed information regarding the structural and functional requirements of the fragments of the anti-EN-RAGE antibody or the fragments of the V-domain of soluble RAGE polypeptide are lacking, it is unpredictable as to which variations, if any, meet the limitations of the claims. Applicant is required to enable one of skill in the art to make and use the claimed invention. In the instant case, while the claims encompass methods using fragments of the anti-EN-RAGE antibody and methods using fragments of the V-domain of soluble RAGE polypeptide, the specification only teaches one skilled in the art to test for polypeptide fragments that interfere with the interaction between EN-RAGE and RAGE. Since the claims do not enable one of skill in the art to make and use the claimed polypeptide fragments, and since detailed information regarding the functional requirements of the polypeptides fragments are lacking, it is unpredictable as to which variations, if any, meet the limitations of the claims. Thus, since Applicant has only taught how to use polypeptide fragments that interfere with the interaction between EN-RAGE and RAGE, it would require undue experimentation of one of skill in the art to practice the method as claimed. This rejection could be obviated by adding as functional limitation for the fragment of anti-EN-Rage wherein the fragment is a binding fragment, and adding a functional limitation for the fragment of the V-domain of soluble

RAGE polypeptide wherein the fragment of the V-domain of soluble RAGE polypeptide binds AGE.

Claims 1-17 are rejected, under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Applicant is directed to the Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001.

The claims are drawn to a method for inhibiting inflammation in a subject which comprises administering to the subject a compound selected from the group consisting of: an anti-EN-RAGE antibody or fragment thereof and the V-domain of soluble RAGE polypeptide or fragment thereof, thereby inhibiting inflammation in a subject. Since the claims are drawn to methods using fragments of anti-EN-RAGE antibody or fragments of V-domain of soluble RAGE polypeptide, the claims thus encompass methods using a genus of variant polypeptides. The written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant identifying characteristics, i.e. structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between structure and function structure, or by a combination of such identifying characteristics,

sufficient to show the applicant was in possession of the claimed genus. In the instant case, the specification fails to provide a correlation between the structure of the fragments and the function set forth in the claim, i.e. inhibiting inflammation in a subject. One of skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species to describe the genus. Thus, applicant was not in possession of the claimed genus. This rejection could be obviated by adding as functional limitation for the fragment of anti-EN-Rage wherein the fragment is a binding fragment, and adding a functional limitation for the fragment of the V-domain of soluble RAGE polypeptide wherein the fragment of the V-domain of soluble RAGE polypeptide binds AGE.

***Conclusion***

No claims are allowed.

The Art Unit location of your application in the USPTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Art Unit 1649.

***Advisory Information***

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gregory S. Emch whose telephone number is (571) 272-8149. The examiner can normally be reached on Monday through Friday from 8:30AM to 5PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Janet L. Andres can be reached at (571) 272-0867. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Gregory S. Emch, Ph. D.
Patent Examiner
Art Unit 1649
July 6, 2005

JOSEPH MURPHY
PATENT EXAMINER